Scientific Abstract

A Phase I Study of Vaccination with Lethally Irradiated, Autologous Acute Myeloblastic Leukemia Cells Engineered by Adenoviral Mediated Gene Transfer to Secrete Human Granulocyte-Macrophage Colony Stimulating Factor

This clinical trial for patients with advanced myelodysplasia or acute myelogenous leukemia (AML) will investigate the use as therapeutic vaccines of autologous, irradiated tumor cells engineered by adenoviral mediated gene transfer to secrete human granulocyte-macrophage colony stimulating factor (GM-CSF). A total of 25 evaluable patients will be treated at three different dose levels of vaccine. Each patient will receive inoculations of either $1x10^6$, $4x10^6$, or $1x10^7$ autologous, GM-CSF secreting acute myeloblastic cells subcutaneously and intradermally. Vaccinations will be given weekly times three and then every two weeks until the supply is exhausted.

The proposed study is based on pre-clinical experiments in murine tumor model systems which indicated that injection of irradiated tumor cells engineered to secrete murine granulocyte-macrophage colony stimulating factor generated potent, specific, and long lasting anti-tumor immunity. Efficacy of irradiated, GM-CSF expressing cells could be demonstrated in models of acute leukemia, lung carcinoma, melanoma, renal cell carcinoma, colon carcinoma, bladder carcinoma, prostate carcinoma, sarcoma, neuroblastoma, glioma, and lymphoma. Three Phase I clinical trials of vaccination with autologous, lethally irradiated tumor cells engineered by retroviral or adenoviral mediated gene transfer to secrete GM-CSF has confirmed these studies in patients with metastatic melanoma and nonsmall cell lung carcinoma; the trials have demonstrated the induction of anti-tumor immunity without significant toxicity. In this study, we will attempt to expand these principles to advanced myelodysplasia or AML. In this trial, harvested myeloblastic cells will be prepared to single cell suspension, infected with an adenovirus expressing human GM-CSF, irradiated, and cryopreserved.

The overall goals of the proposed phase I study are:

1. To determine the feasibility of preparing autologous, lethally irradiated, acute myeloblastic cells engineered by adenoviral mediated gene transfer to secrete GM-CSF in patients with advanced myelodysplasia or AML.

2. To determine the safety and biologic activity of vaccination with autologous, lethally irradiated acute myeloblastic cells engineered by adenoviral mediated gene transfer to secrete GM-CSF in patients with advanced myelodysplasia or AML.